

# Exhibit C



## **COVID-19 Treatment Guidelines**

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# Overview of COVID-19

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## Epidemiology

The COVID-19 pandemic has exploded since cases were first reported in China in December 2019. As of December 5, 2020, more than 66 million cases of COVID-19 — caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection — have been reported globally, including more than 1.5 million deaths.<sup>1,2</sup>

Individuals of all ages are at risk for infection and severe disease. However, the probability of serious COVID-19 disease is higher in people aged  $\geq 60$  years, those living in a nursing home or long-term care facility, and those with chronic medical conditions. In an analysis of more than 1.3 million laboratory-confirmed cases that were reported in the United States between January and May 2020, 14% of patients required hospitalization, 2% were admitted to the intensive care unit, and 5% died.<sup>3</sup> The percentage of patients who died was 12 times higher (19.5% vs. 1.6%) and the percentage of patients who were hospitalized was six times higher (45.4% vs. 7.6%) in those with reported medical conditions than in those without medical conditions. The mortality rate was highest in those aged  $>70$  years, regardless of the presence of chronic medical conditions. Among those with available data on health conditions, 32% had cardiovascular disease, 30% had diabetes, and 18% had chronic lung disease. Other conditions that may lead to a high risk for severe COVID-19 include cancer, kidney disease, obesity, sickle cell disease, and other immunocompromising conditions. Transplant recipients and pregnant people are also at a higher risk of severe COVID-19.<sup>2,4-10</sup>

Emerging data from the United States suggest that racial and ethnic minorities experience higher rates of COVID-19 and subsequent hospitalization and death.<sup>11-15</sup> However, surveillance data that include race and ethnicity are not available for most reported cases of COVID-19 in the United States.<sup>2,16</sup> Factors that contribute to the increased burden of COVID-19 in these populations may include over-representation in work environments that confer higher risks of exposure to COVID-19, economic inequality (which limits people's ability to protect themselves against COVID-19 exposure), neighborhood disadvantage,<sup>17</sup> and a lack of access to health care.<sup>16</sup> Structural inequalities in society contribute to health disparities for racial and ethnic minority groups, including higher rates of comorbid conditions (e.g., cardiac disease, diabetes, hypertension, obesity, pulmonary diseases), which further increases the risk of developing severe COVID-19.<sup>15</sup>

## Clinical Presentation

The estimated incubation period for COVID-19 is up to 14 days from the time of exposure, with a median incubation period of 4 to 5 days.<sup>6,18,19</sup> The spectrum of illness can range from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome (ARDS) and death. Among 72,314 persons with COVID-19 in China, 81% of cases were reported to be mild (defined in this study as no pneumonia or mild pneumonia), 14% were severe (defined as dyspnea, respiratory frequency  $\geq 30$  breaths/min, saturation of oxygen [SpO<sub>2</sub>]  $\leq 93\%$ , a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen [PaO<sub>2</sub>/FiO<sub>2</sub>]  $<300$  mm Hg, and/or lung infiltrates  $>50\%$  within 24 to 48 hours), and 5% were critical (defined as respiratory failure, septic shock, and/or multiorgan dysfunction or failure).<sup>20</sup> In a report on more than 370,000 confirmed COVID-19 cases with reported symptoms in the United States, 70% of

patients experienced fever, cough, or shortness of breath, 36% had muscle aches, and 34% reported headaches.<sup>3</sup> Other reported symptoms have included, but are not limited to, diarrhea, dizziness, rhinorrhea, anosmia, dysgeusia, sore throat, abdominal pain, anorexia, and vomiting.

The abnormalities seen in chest X-rays vary, but bilateral multifocal opacities are the most common. The abnormalities seen in computed tomography of the chest also vary, but the most common are bilateral peripheral ground-glass opacities, with areas of consolidation developing later in the clinical course.<sup>21</sup> Imaging may be normal early in infection and can be abnormal in the absence of symptoms.<sup>21</sup>

Common laboratory findings in patients with COVID-19 include leukopenia and lymphopenia. Other laboratory abnormalities have included elevated levels of aminotransferase, C-reactive protein, D-dimer, ferritin, and lactate dehydrogenase.

While COVID-19 is primarily a pulmonary disease, emerging data suggest that it also leads to cardiac,<sup>22,23</sup> dermatologic,<sup>24</sup> hematological,<sup>25</sup> hepatic,<sup>26</sup> neurological,<sup>27,28</sup> renal,<sup>29,30</sup> and other complications. Thromboembolic events also occur in patients with COVID-19, with the highest risk occurring in critically ill patients.<sup>31</sup>

The long-term sequelae of COVID-19 survivors are currently unknown. Persistent symptoms after recovery from acute COVID-19 have been described (see [Clinical Spectrum of SARS-CoV-2 Infection](#)). Lastly, SARS-CoV-2 infection has been associated with a potentially severe inflammatory syndrome in children (multisystem inflammatory syndrome in children, or MIS-C).<sup>32,33</sup> Please see [Special Considerations in Children](#) for more information.

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